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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/446,634	12/23/1999	HIROSHI HAGIYA	Q57282	2661

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SUGHRUE MION ZINN MACPEAK & SEAS
2100 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20037

EXAMINER

YU, MISOOK

ART UNIT PAPER NUMBER

1642

DATE MAILED: 02/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/446,634

Applicant(s)

HAGIYA ET AL.

Examiner

MISOOK YU, Ph.D.

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 20 and 24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 20 and 24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 03/11/03, 8/1/00
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: Notice to Comply, Self Alignment

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/19/2003 and 11/19/2003 have been entered.

Claims 1-4, 20, and 24 are pending, and examined on merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This Office action contains new grounds of rejection.

Priority

In response to applicant's request, acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d).

Information Disclosure Statement

The information disclosure statement filed 3/11/2003 and 08/26/2000 have been considered except Document No. 9-50411 (JP) and a signed and initialed copy of the lists (1449) are attached with this Office action. Document No. 9-50411 (JP) is in Japanese and the Examiner is not able to understand the content of the document.

The information disclosure statement does not include a concise explanation of the relevance Document No. 9-50411 (JP), as it is presently understood by the

individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of Document No. 9-50411 (JP) that is not in the English language. It has been placed in the application file, but Document No. 9-50411 (JP) has not been considered.

Claim Rejections - 35 USC § 112

The rejection of claim 20 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn in view of the amendment.

***The Following Are New Grounds of Rejection
Specification***

The disclosure is objected to because of the following informalities: This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. The specification has antigen-originated nuclear transport signal (Ala Pro Lys Lys Lys Arg Lys Val Gly) at page 25 line 1. The sequence listing submitted on 03/11/2003 does not contain the sequences. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Allowable Subject Matter

The indicated allowability of claims 1-4 is withdrawn in view of the newly discovered primary reference(s) to US Pat. 5,972,899 (Zychlinsky et al, issued Oct. 26,

1999 with filing date of Jan. 25, 1996). Rejections based on the newly cited reference(s) follow.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat. 5,972,899 (Zychlinsky et al, issued Oct. 26, 1999, filed date of Jan. 25, 1996).

Claim 1 is interpreted as drawn to a plasmid DNA comprising Gal4 responsive element, a promoter, and a polynucleotide encoding a transmembrane region and an apoptosis-inducing domain of a Fas in 5' to 3' direction such that said transmembrane region and said apoptosis-inducing domain of Fas is expressed by activation of said Gal4 responsive element, and said promoter. Based on the open language "comprising" in the instant claim, the claim is interpreted as open in terms of a Fas sequence.

The art (US Pat. 5,972,899) teaches Gal4 responsive element and promoter at column 13, line 41, and column 10 line 65, and also teaches, at column 8 lines 19-38 column 11 lines 12-13, a Fas antigen which obviously has a transmembrane and a apoptosis-inducing domain, thus teaching every limitation of the instant claim. Further, US Pat. 5,972,899 teaches at the abstract that activation of apoptosis is useful in treating cancer and other diseases; also teaches at column 8, lines 30-35 that Fas, ICE,

and IpaB all induces apoptosis in that stimulation of Fas activates ICE which is a target of IpaB (new discovery disclosed in the art); also teaches at column 13 lines 26-46 that "one means for inducing apoptosis in a controlled manner is to use an IpaB DNA construct in combination" with estrogen-inducible system controlled by GAL4-responsive promoter which is transactivated in presence of 17- β estradiol by the fusion protein comprising DNA-binding domain of GAL4 and the ligand binding domain of estrogen receptor. The only difference between the inducible system for inducing apoptosis disclosed at column 13 lines 26-46 of the art and the instantly claimed plasmid construct is the apoptois-causing fragment of the construct; the art uses DNA encoding IpaB and while the instant claim uses polynucleotide encoding a transmembrane region and an apoptosis-inducing domain of a Fas in order to accomplish apoptosis in a controlled manner using Gal4 responsive element and a promoter. However, the art teaches IpaB and Fas are functionally equivalent i.e. both induce apoptosis. Note column 8 lines 30-35.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make and use a plasmid construct Gal4 responsive element, a promoter, and a polynucleotide encoding a transmembrane region and an apoptosis-inducing domain of a Fas in 5' to 3' direction such that said transmembrane region and said apoptosis-inducing domain of Fas is expressed by activation of said Gal4 responsive element, and said promoter for use in regulating apoptosis since the art teaches that IpaB and Fas are functional equivalents i.e., both regulates apoptosis.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat. 5,972,899, and further in view of any one of Oehm et al (1992, J. Biol. Chem., vol. 267, pages 10709-15), Adach et al (Proc. Natl. Acad. Sci. USA, vol. 90, pages 1756-60), or Itoh et al (1991, Cell, vol. 66, pages 233-43).

The claims are interpreted as drawn to plasmid DNA comprising the enhancer and promoter i.e., Gal4 responsive element, a promoter, and a polynucleotide encoding either SEQ ID NO:22 (human Fas) or SEQ ID NO:23 (mouse Fas) because of the open language in the base claim.

The primary reference (US Pat. 5,972,899) teaches plasmid DNA comprising the enhancer and promoter i.e., Gal4 responsive element, a promoter, and Fas. Note rejection of claim 1 above.

The primary reference does not teach SEQ ID NO:22 or 23.

However, any one of the three secondary references teaches SEQ ID NO:22 or 23, which is a Fas amino acid sequence. Oehm et al teach that Fas antigen had been cloned and the clone had been deposited as GenBank Accession number X63717 well before the effective filing date of the instant application (note the attached sequence alignment of instant SEQ ID NO:22). Adach et al teach at Fig. 2 that mouse Fas antigen had also been cloned well before the effective filing date of the instant application (note the attached sequence alignment of instant SEQ ID NO:23). Itoh et al teach at Fig. 2 a human Fas antigen sequence (note the attached sequence alignment of instant SEQ ID NO:22).

One of ordinary skill in the art would have been motivated and have a reasonable expectation of success in making and using the instantly claimed plasmid DNA construct comprising Gal4 responsive element, a promoter, and a polynucleotide encoding either SEQ ID NO:22 (human Fas) or SEQ ID NO:23 (mouse Fas) because the primary reference teaches usefulness of such plasmid construct in inducing controlled apoptosis (note the rejection of claim 1 above for further detail). In addition, it would have been obvious because the primary reference teaches that IpaB and Fas are functional equivalents. Thus, it would have been obvious to replace IpaB with SEQ ID NO:22 or 23 taught by any one of the secondary reference in order to make and use the claimed plasmid construct. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Claims 1, 20 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat. 5,972,899, and further in view of Braselmann et al (Proc Natl Acad Sci U S A. 1993 Mar 1;90(5):1657-61).

The claims are interpreted as drawn to composition comprising (a) the plasmid DNA of claim 1 and (b) a plasmid DNA encoding a fusion protein comprising in a 5' to 3' direction a Gal4 DNA binding region and a nuclear receptor ligand binding region, more specifically amino acid 281 to 595 of human estrogen receptor.

The primary reference teaches (a) plasmid. Note the rejection of claim 1 above but the primary reference does not teach (b) plasmid above.

However, Braselmann et al teach at Fig. 5 a plasmid DNA encoding a fusion protein comprising in a 5' to 3' direction a Gal4 DNA binding region and a nuclear receptor ligand binding region, more specifically amino acid 281 to 595 of human estrogen receptor, thus Braselmann et al teaches (b) plasmid above. Further, Braselmann et al teach, at page 1657, right column, first paragraph that "steroid receptors belong to a family of ligand-inducible transcription factors with separable DNA and hormone binding domains" and the hormone binding region of human estrogen receptor could be used to stimulate transcription from Gal4-responsive gene in a hormone-dependent manner.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make and use the instant claimed invention to activate apoptosis by activating transcription of Fas controlled by binding of the fusion protein (Gal4-a nuclear receptor ligand binding region, more specifically estrogen receptor hormone comprising amino acids 281-595) in presence of 17- β estradiol. One in ordinary skill would have been motivated to make and use the plasmid constructs in the claimed composition with a reasonable expectation of success because the art as whole teaches that inducing apoptosis in controlled manner is useful and could be accomplished in presence of 17- β estradiol.

Claims 1, 20, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat. 5,972,899, and further in view of Braselmann et al (Proc Natl Acad Sci U S A. 1993 Mar 1;90(5):1657-61), and further in view of the instant specification at the paragraph bridging page 11-12.

The claim is interpreted as drawn to composition comprising (a) the plasmid of claim 1 and (b) a plasmid DNA encoding a fusion protein comprising in a 5' to 3' direction a Gal4 DNA binding region and the nuclear receptor ligand binding regions recited in the instant claim 24 except amino acid 281 to 595 of human estrogen receptor, which is rejected above.

The primary (the patent), and the secondary references (Braselmann et al) teaches the plasmid of claim 1 and (b) a plasmid DNA encoding a fusion protein comprising in a 5' to 3' direction a Gal4 DNA binding region and a nuclear receptor ligand binding region (amino acids 281-595 of human estrogen receptor) respectively. However, the primary and secondary references do not teach the other nuclear ligand binding region recited in claim 24.

The specification at page 11-12 teaches "the ligand binding region of each receptor" is already known well before the effective filing date of the instant application in Science, 240, 889 (1 988), Mol. Endocrinology, 6, 1634 (1 992), Bibchem. Biophys. Res. Commun., 224, 431 (1996)., J. Steroid Biochem. Molec. Biol., 51 , 157 (1994)., and Proc. Natl. Acad. Sci. USA, 91 , 7355 (1994).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make and use the transcriptional induction construct by fusing Gal4 DNA binding region to a nuclear receptor ligand binding region since Braselmann et al suggest that a nuclear receptor ligand binding region is useful order to regulate transcription and US Pat. 5,972,899 teaches controlled induction of

apoptosis by controlled transcription of apoptosis-inducing protein encoding gene is useful for various diseases such as cancer.

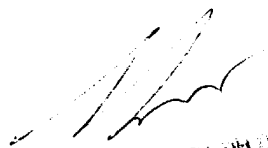
Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne C Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Misook Yu, Ph.D.
February 5, 2004


LARRY R. HELMS, Ph.D.
PRIMARY EXAMINER